REMARKS

Claims 23-30 have been canceled. New claims 31-38 have been added and correspond to prior claims 23-30. Claims 31-38 have been added to more distinctly claim that which Applicant regards as his invention.

1. Substitute Specification

Applicant had submitted a substitute specification along with the response submitted on April 17, 2001. This substitute specification was submitted in response to the objections made to the disclosure in the Office Action dated February 4, 1999. In Applicants' view and in view of the new rules of practice, it was most prudent to submit a substitute specification instead of substitute pages. Any changes made were editorial in nature. No new matter was added. Applicants respectfully request entry of the substitute specification.

1. The Obviousness Type Double Patenting Rejection

Claims 23-30 have been rejected over claims 23-36 of U.S. Patent No. 5,770,355 under the judicially created doctrine of obviousness-type double patenting. It is asserted that the conflicting claims are not patentably distinct from each other because the claims of '355 are directed to a lipid transfer protein and the present claims are more broadly directed to a protein that transports.

Applicant respectfully traverses the rejection. The method for screening for an inhibitor recited in claims 23-26 of the '355 patent requires that an acceptor particle be added to the test solution (see claim 23, step (b). In contrast, the method of the present invention recited in new claims 31-38 (corresponds to prior claims 23-30) comprise the following steps:

(a) obtaining a sample comprising said protein;

(b) incubating said sample with (i) a donor substance labeled with a light emitter wherein light emitted from said light emitter increases with increasing activity of said protein and (ii) an acceptor dependent concentration (claim 31) or a protein dependent concentration (claim 35) light emission intensity quencher, wherein quenching of said light emission intensity increases with concentration of acceptor or protein endogenously present in said sample and wherein said quencher is a normalization factor and

(c) detecting light emission intensity to determine activity of said protein.

Thus, the method of the present invention employs an internal standard, the quencher, which acts as a normalization factor. Given that the method of the present invention contains a quencher which acts as a normalization factor, it would follow that exogenous acceptor is not added. Therefore, new claims 31-38 are patentably distinct from claims 23-36 of U.S. Patent No. 5,770,355. In view of the above arguments, Applicants respectfully request that the obviousness-type double patenting rejection be withdrawn.

2. The Enablement Rejections

Claims 23-30 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is asserted that the application as originally filed does not enable the newly submitted claims that appear to be directed to an assay with some fluorescent component. It would appear there is a chemical reaction cascade involved in the invention but none is shown. The Examiner points out the following specific instances: page 9 last full paragraph, such a method is not understood in context. On page 10 second paragraph last line, it is not seen how CETP mass is measured. On page 11 last paragraph, "the normalization factor includes a colorizing factor that reacts in response to the normalizing factor of choice." The example on page 12 in the Examiner's view, is insufficiently detailed to follow. It is noted that neither data of any sort nor

results of any determination are found in the specification. As written, one of skill in this art could not perform the claimed invention by following the teachings of the specification.

Again, as noted above, Applicant, in response, notes that claims 23-30 have been canceled. New claims 31-38 have been added. The specification, in Applicant's view, does enable new claims 31-38. Each point raised by the Examiner will be specifically addressed.

First page 9, last paragraph provides support for step (b)(I) of claims 31 and 35. This paragraph provides an example of a donor substance, specifically a CE donor labeled with a light emitter, here a fluorescer, where the fluorescence increases with increased activity of protein in the sample, which in the example on page 9 is CETP.

Second , the last paragraph of page 10 provides a sufficient description for measuring **CETP activity**. Applicants wish to emphasize that it is CETP activity not mass that is being measured. It is noted that when no exogenous acceptor or normalization factor is added, CETP activity may appear to be higher even though there is no change in the amount (mass) of CETP present.

With respect to page 11, last paragraph, a sufficient description of the normalization factor is provided on page 12.

Finally, Applicant asserts that sufficient detail was provided on page 12 regarding the method of the present invention. It is certainly not required that Applicant provide data in the specification. MPEP §2604.02, attached hereto states "Compliance with the enablement requirement of 35 U.S.C. §112, first paragraph does not turn on whether an example is disclosed. ...An applicant need not have actually reduced the invention to practice prior to filing (citation omitted).".Applicant asserts that one of ordinary skill in the art could perform the claimed invention following the teachings of the specification. The fact that experimentation may be involved in making this determination, even if it may be time-consuming and laborious, it is not fatal, provided that the experimentation is routine, and does not require the exercise of inventive skill. *In re Wands,* 8 USPQ 2d

(Fed. Cir. 1988); *Fields v. Conover*, 170 USPQ 276 (CCPA 1971). A sufficient description of an embodiment of the present invention is provided in the paragraph bridging pages 13 and 14 in the instant application.

3. The Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 23-30 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is asserted that in claim 23(b), "an acceptor dependent concentration light emission intensity quencher" is not understood in context and "of said light emission intensity" lacks antecedent basis. It is also asserted that "a normalization factor" in context is not understood as to what it is and what it does. It is asserted that claim 23 is directed to measuring activity but lacks any such step to perform that function and lacks any correlating step; claim 24 "the donor particle" lacks antecedent basis; claim 25 is not understood and in claim 27(ii) "a protein dependent concentration light emission intensity quencher" is not understood in context.

In response, as noted above, claims 23-30 have been canceled. New claims 31-38 have been added. First, Applicants note that step (b) in claim 31 recites that sample is incubated with (i) a donor substance labeled with a light emitter wherein light emitted from said light emitter increases with increasing activity of said acceptor and (ii) a light emission intensity quencher, wherein quenching of said light emission intensity by said quencher increases with concentration of acceptor present in said sample. New claim 32 recites that the **donor substance** comprises a fluorescent lipid.

Further terms in question in prior claims 23, 25 and 27 (now claims 21, 22 and 35) are easily understood when read in context of the specification. It is well-established case law that the words of a claim cannot be read in a vacuum but rather must be read in light of the specification and what is known in the art. *In re Moore*, 169 USPQ 236 (CCPA 1971). "A normalization factor" as noted above is described on page 10, last paragraph:

> The present invention accounts for variable lipoprotein profiles by normalizing with a color development reaction in

> response to cholesterol and/or triglyceride and/or phospholipid and/or protein. The development of color creates a quenching effect upon the fluorescence of the CE. Therefore, the greater the concentration of CE/TG/PL/protein the greater is the color quenching effect upon the fluorescent label. This normalizes the fluorescent intensity for LDL concentration.

Step (c) is directed to detecting light emission intensity to determine activity of said protein. The activity of the protein is therefore determined by detecting light emission intensity. The relationship between light emission intensity and protein activity is described in the specification on page 6, last paragraph, where it is specifically stated.

> The activity parameter is established with a light emitting measurement technique that includes fluorescent and chemiluminescence enzyme activity assays where the protein activity is assessed by a fluorimeter or luminometer as a change in light emission intensity.

Claim 25 can easily understood in view of page 12, lines 12-17:

> The higher the concentration of the C/CE from the endogenous plasma lipoproteins, the darker the color from the colorimetric assay. Increased color decreases the measurable fluorescence intensity of the activity assay due to color quenching of the fluorescent label thereby normalizing the results according to the endogenous lipoproteins present in the plasma.

And page 14, lines 2-4.

> The normalization may be based on colorimetric techniques utilizing TG and CE due to the presence of endogenous lipoproteins in the sample.

Thus, while the above-referenced terms read on their own may not be clear, when read in the context of the specification and the plain meaning of the word as it is understood by those skilled in the art, it is unquestionably definite as to what is intended.

In view of new claims 31-38 and the above arguments, Applicants assert that the rejections under 35 U.S.C. §112, second paragraph have been overcome. Therefore, Applicants respectfully request that the rejections be withdrawn.

4. Miscellaneous

The title of the invention is not aptly descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. In response, a new title is provided in the Substitute Specification.

5. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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